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Health and Medicine Division

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## ***Standing Committee on Emerging Infectious Diseases and 21st Century Health Threats***

Meeting #1: March 11, 2020

**Recap of Research Topics Discussed at the Meeting Among OSTP, ASPR, and Committee**

This list of research topics was compiled based on discussions held at the first meeting of the Standing Committee On Emerging Infectious Diseases and 21st Century Health Threats, as well as from a list of topics submitted by the sponsors (OSTP and HHS/ASPR) and a list of topics submitted by the committee prior to the first meeting. Please note this is a first cut at many of the very important questions regarding the current COVID-19 outbreak, if you would like to submit additional questions or topics, please submit them to SCEID@nas.edu.

Overall, a clear need exists to develop a framework to prioritize actions and determine what should be taking place in parallel, rather than serially, in response to emerging infectious diseases and the current COVID-19 outbreak.

**Virus Characteristics**

- *Virus genetics, origin, and evolution*
  - Short-term
    - Real-time tracking of whole genomes and a mechanism for coordinating the rapid dissemination of that information to inform the development of diagnostics and therapeutics.
    - Access to geographic and temporal diverse sample sets to understand geographic distribution and genomic differences. Multi-lateral agreements such as the Nagoya Protocol could be leveraged.
    - Efforts to determine whether there is more than one strain in circulation, and if so, what is the difference in virulence and transmissibility.
  - Long-term

        - Determine if there is a genetic sequence (receptor binding) evidence that livestock could be infected and serve as a reservoir after the epidemic appears to be over. This could potentially result in food security issues.
            - Is there field surveillance evidence for the involvement of livestock in either the origins of the outbreak or current circulation of the virus? Is there evidence of farmers being infected, and could they have played a role in the origin? What surveillance of mixed wildlife- livestock farms has been conducted for SARS-CoV-2 and other coronaviruses in Southeast Asia? Have experimental infections been conducted to test host range for this pathogen?
        - Employ better One Health surveillance of humans and potential sources of future spillover or ongoing exposure for this organism and future pathogens, including both evolutionary hosts (e.g., bats) and transmission hosts (e.g., heavily trafficked and farmed wildlife and domestic food and companion species), inclusive of environmental, demographic, and occupational risk factors.
            - Develop alternatives and incentives to move away from wildlife markets.
- *Transmission, incubation, and environmental stability*
    - Short-term
        - Need to understand the range of incubation periods for the disease in humans (and how this varies across age and health status) and how long individuals are contagious, even after recovery.
        - Important to understand the prevalence of asymptomatic shedding and transmission (e.g., particularly children).
        - Need to better understand the seasonality of transmission.
        - The physical science of the coronavirus should be studied/better understood (e.g., charge distribution, adhesion to hydrophilic/phobic surfaces).
        - Important to understand environmental survival and how long the virus remains infectious on a variety of surfaces to inform decontamination efforts for affected areas and provide information about viral shedding. Also important to understand the persistence and stability on a multitude of substrates and sources (nasal discharge, sputum, urine, fecal matter, blood).
- *Risk factors*
    - Short-term
        - Data on risks factors for besides age
            - Smoking, pre-existing pulmonary disease
            - Co-infections (determine whether co-existing respiratory/viral infections make the virus more transmissible or virulent) and other health conditions
            - Neonates and pregnant women
            - Socio-economic and behavioral factors

**Diagnostics and Surveillance**

- *Systematic, holistic approach to diagnostics (from the public health surveillance perspective to being able to predict clinical outcomes)*
    - Short-term
        - Explore efforts to increase capacity on existing diagnostic platforms and tap into existing surveillance platforms. Recruit, support, and coordinate local expertise and capacity (public, private—commercial, and non-profit, including academic). There



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are obvious legal, ethical, communications, and operational issues that need to be considered; thus, it may be useful to issue national guidance and guidelines about best practices to states suggesting they leverage their universities and private laboratories for testing purposes as well as other important functions (with good communications to public health officials).

- Need denominators for testing and a mechanism for rapidly sharing that information, including demographics, to the extent possible. Consider whether serosurveys (convalescent samples) could be used to determine how much asymptomatic disease there is in the U.S. or whether use of screening of neutralizing antibodies for early detection (e.g. ELISAs) could be used.

- With the increasing emphasis on the current clinical testing methodology and its logistical challenges, it is clear that the development of a point-of-care test (like a rapid influenza test) and rapid bed-site tests would be valuable additions to both the clinical and public health diagnostic/surveillance missions.
  - Understand tradeoffs between speed, accessibility, and accuracy.
- Targeted surveillance experiments could be rapidly designed and executed calling all potential testers using PCR in a defined area to start testing and report to a specific entity. These experiments could aid in collecting longitudinal samples, which are critical to understanding the impact of ad hoc local interventions (which also need to be recorded).
- Need to separate assay development issues from instruments. There are many instruments that could be leveraged, but we need the private sector to help quickly migrate assays onto those devices.
- Establish efforts to not lose track of the evolution of the virus (i.e., genetic drift or mutations). Avoid locking into specific reagents and surveillance/detection schemes.
- Enhance understanding of latency issues and when there is sufficient viral load to actually detect the pathogen, and understanding of what is needing in terms of biological and environmental sampling.
- As we move into the treatment phase, use diagnostics to look at disease progression. Determine whether there are host response markers (e.g., cytokines) that may be able to detect early disease or predict severe disease progression. These tests are important to understanding best clinical practice and efficacy of therapeutic interventions.
- Build knowledge of the frequency, manifestations, and course of extrapulmonary manisfestations of COVID-19, including, but not limited to, possible cardiomyopathy.

- Long-term
  - Technology roadmap for diagnostics.
  - Identify the barriers to developing and scaling up new diagnostic tests (e.g., market forces) and discuss future coalition and accelerator models (e.g., Coalition for Epidemic Preparedness Innovations) to provide critical funding for diagnostics, and discuss opportunities for a streamlined regulatory environment.
  - Discuss new platforms and technology (e.g., CRISPR) that will be useful beyond COVID-19 and be ready for the next Disease X to improve future response times and employ more holistic approaches.
  - Work towards coupling genomics and diagnostic testing on a large scale.



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        - Enhance capabilities for rapid sequencing and bioinformatics to target regions of the genome that will allow specificity for a particular variant.
        - Enhance capacity for sequencing with advanced analytics for unknown pathogens, and explore capabilities for distinguishing naturally-occurring pathogens from intentional.

**Medical Care**

- *Surge capacity and nursing homes*
    - Short-term
        - The neglect of SNF/LTCF is a critical vulnerability in the health care system. Determine how to address this effectively.
        - Mobilizing surge medical staff from the outside community is also a significant hurdle that needs to be overcome.
- *Efforts to inform allocation of scarce resources*
    - Short-term
        - Data needs on:
            - age-adjusted mortality data for Acute Respiratory Distress Syndrome (ARDS) with/without other organ failure – particularly for viral etiologies
            - extracorporeal membrane oxygenation (ECMO) outcomes of COVID-19 patients; and,
            - outcomes for COVID after mechanical ventilation adjusted for age.
        - Consider whether it make senses to apply some of these same regulatory standards (EUA, CLIA). Adapt care to crisis standards of care level.
- *PPE*
    - Short-term
        - Consider encouraging and facilitating the production of elastomeric respirators, which can save thousands of N95 masks.
- *Alternate methods to advise on disease management*
    - Short-term
        - Learn from current best practices in telemedicine, and explore barriers and faciltators to more reapid deployment.
        - Provide guidance on the simple things people can do at home to take care of sick people and manage disease. Examine oral medications that might potentially work.
    - Long-term
        - How can we better utilize AI to at medical care of the cases in real-time? AI can look at interventions, risk factors, and outcomes in a way that cannot be done manually.
- *Processes of care*
    - Short-term
        - Examine innovations in hospital flow and organization, workforce protection, workforce allocation, community-based support resources, payment, and supply chain management.

**Non-Pharmaceutical Interventions**

- *Effectiveness*
    - Short-term
        - Guidance on ways to scale up NPIs in a more coordinated way to give us time to enhance our health care delivery system capacity to respond to an increase in cases.



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        - Rapidly design and execute experiments to examine and compare NPIs currently being implemented. This will require the involvement of evaluation scientists. DHS Centers for Excellence could potentially be leveraged to conduct these experiments.
        - Rapid assessment of the likely efficacy of school closures, travel bans, bans on mass gatherings of various sizes, and other social distancing approaches.
- *Equity and barriers to compliance*
    - Short-term
        - Science is needed to determine what it will take to control the spread in communities, but understanding the barriers to compliance and how these vary among different populations is equally important.
        - Ensure that models that are constructed to inform recommendations and communication that look at potential interventions factor in barriers (race, income, disability, age, geographic location, immigration status, housing status, employment status- wage, gig etc, health insurance status) so that they can truly predict benefits and costs of various approaches.
        - Explore policy short- (and long-) term changes to ensure the compliance of individuals with limited resources and the underserved with NPIs. The idea that people fail to comply with public health advice, even if they want to, because the social costs and financial cost may be too high, is one that should not be subsumed solely under the heading of behavioral science research.

**Vaccines & Therapeutics**

- *Research and development and evaluation efforts*
    - Short-term
        - Determine whether there is any indication yet that drugs being tried are effective.
            - It is important to understand clinical and bench trials to investigate less common viral inhibitors against COVID such as naproxen, clarithromycin, minocycline, and others that exert effects on viral replication.
        - With many vaccine development efforts underway, some driven by the US Government, determine how best to evaluate for the potential complication of Antibody-Dependent Enhancement (ADE) in vaccine recipients.
            - Determine what should be considered from a clinical development perspective. Is there consensus on the best animal models and their predictive value for a human vaccine?
        - Enhance capabilities to discover a therapeutic (not vaccine) for the disease.
        - Systems to ensure equitable access to therapeutics (antiviral agents) when they become available need to be set up pre-emptively.
    - Long-term
        - Efforts targeted at a universal coronavirus vaccine.

**Risk Communication**

- *Communicating with high-risk populations*
    - Short-term
        - Target high-risk populations (elderly, health care workers) with specific communication.
- *Clarify community measures*
    - Short-term



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- Clarify misunderstanding around containment vs. mitigation.

**Equity Considerations**

- *Problems of inequity*
  - Short-term
    - Understand and mitigate problems of inequity of access to information, surveillance, treatment and support as a result of racial, socio-economic, linguistic, geographic, and other disparities.
    - Develop and support measures to reach marginalized and disadvantaged populations.
    - Assure that data systems and research priorities and agendas incorporate attention to the needs and circumstances of disadvantaged populations and underrepresented minorities.
    - Understand and mitigate *threats* to incarcerated people from COVID-19, assuring access to information, prevention, diagnosis, and treatment.

**Information Sharing & Inter-sectoral Collaboration**

- *Data standards and nomenclature*
  - Short-term
    - Establish coordinated data-gathering with standardized nomenclature.
    - Establish a consistent platform for sharing response information among planners, providers, etc.
    - Understand and mitigate barriers to information-sharing.
- *Governmental public health*
  - Short-term
    - Determine how to recruit, support, and coordinate local (non-Federal) expertise and capacity relevant to bio emergency response (public, private—commercial and non-profit, including academic).
  - Long-term
    - Better integrate state/local public health systems with such capacity in the long term. We need more investments in baseline preparedness/public health infrastructure.

**Evaluation and Research to Inform Future Efforts**

- Now is the time to use the tools at our disposal, as well as global momentum and motivation, to drastically improve our understanding of the viral diversity and risk factors for viruses that are not yet known to medicine but exist and are available to infect humans and present epidemic and pandemic threats, so that we can be better prepared and reduce panic in the future.